BMJ

LONDON, SATURDAY 16 JULY 1994

Chernobyl, childhood cancer, and chromosome 21

Probably nothing to worry about

In 1986 the accident at the nuclear reactor in Chernobyl in the former Soviet Union released large amounts of radioactivity into the atmosphere. Adjacent areas were heavily contaminated, while more distant regions were affected less. International committees concluded that valuable information on the effects of radiation might result from long term follow up of workers affected by the accident, many of whom received doses in the range of 250-1000 mSv. The committees also recommended that studies should be carried out of residents living within a 30 km radius of the reactor and of residents of substantially contaminated regions in Belarus, the Ukraine, and Russia, who may have received doses of 50-60 mSv. The scientific value of investigations in Europe and other parts of the former Soviet Union was questioned, however, because estimated exposures (<1 mSv) were believed to have been too low to cause a detectable excess of cases of cancer or genetic defects.[1] For comparison, annual doses from natural background radiation are 1-2 mSv.[2]

Nevertheless, because of widespread concern among populations in Europe living in areas of low fallout, the International Agency for Research on Cancer organised the European childhood Ieukaemia-lymphoma incidence study using population based cancer registries in 20 countries. Preliminary results at the end of 1988 showed no increase in childhood leukaemia, but the follow up was probably too short.[3] Results of extended follow up of cancer registries to the end of 1992 in two countries participating in the European study, Finland and Sweden, are published in this week's journal (p 151, p 154)[4,5] and essentially report negative results, similar to those of a recent study of heavily contaminated regions in Belarus.[6]

While these reports may calm public anxieties, such descriptive (ecological) studies are inherently limited. Ecological studies focus on groups rather than individuals as the unit of observation and evaluate variations in the distribution of disease over geographical regions or time. Because exposures cannot be correlated with disease in the same person and because confounding factors cannot be adequately controlled for, such studies are especially prone to bias.[7] Thus, higher rates of cancer in regions with greater radiation contamination cannot be ascribed with certainty to the exposure related to the accidents Ecological studies are useful for generating hypotheses but are of limited value in testing hypotheses or quantifying risks of cancer associated with environmental exposures.

Studies of low doses also have limited statistical power to detect effects.[9] Although radiation can cause leukaemia, our accumulated knowledge would lead us to conclude beforehand that the tiny doses received in Scandinavia were much too small for an excess of cases to be expected.[1] Even in Finland the estimated dose of radiation from Chernobyl was only 0.4 mSv,[4] whereas the estimated cumulative natural background dose was 6-12 mSv during 1987-92. While the absence of an effect from radiation is unsurprising, the wide confidence intervals preclude the rejection of the small effect predicted because of the low doses involved. Paradoxically, if a significant result was found at such low doses our cumulative experience with cancer related to radiation might lead us to treat the observation as a chance (or biased) occurrence.[9]

A third ecological study in this week's journal describes an apparent cluster of cases of Down's syndrome in Berlin, based on two cases that were diagnosed prenatally and 10 cases that were diagnosed in newborn infants, which occurred about nine months after the accident at Chernobyl (p 158).[10] An earlier report of this finding was previously criticised, ' and this finding was not confirmed in subsequent larger and more representative series in Europe.[11] The authors dismiss too easily or fail to consider other explanations and several possible sources of bias. The effects of increased medical surveillance. (shown by the notably sharper increase in prenatal diagnoses between 1986 and 1987 than in earlier or later periods) and possible reporting biases after the accident at Chernobyl are not discussed. The disproportionate occurrence of Down's syndrome among males in the Berlin study is peculiar since preconceptional radiation might be expected to reduce the number of male offspring. Trisomy 21 is significantly associated with maternal age, but no adjustment for this was made in the analysis. Furthermore, it is improbable that the very low doses in Berlin would result in a detectable excess while the higher doses in other parts of Europe did not. " The Berlin study is also inconsistent with studies of children of Japanese survivors of the atomic bombs, in whom no genetic anomalies, including Down's syndrome, were found in excess.[12] Analytical epidemiological studies of high dose maternal irradiation before conception are also equivocal.[2]

The special difficulties in evaluating, ecological findings are further exemplified in a recent survey in Norway in which the risk of Down's syndrome fell with increasing levels of estimated radiation from Chernobyl.[13] Because misclassification of exposure and inadequate control of important cofactors can lead to spurious associations, both positive and negative, ecological analyses must be interpreted with great caution.

The importance of studies of human populations exposed to radiation from Chernobyl is not to prove that radiation causes cancer: this has been accepted for more than 50 years, and risks are remarkably well quantified.[2] Rather, the studies with individual dose characterisations might provide new information on the effects of exposure accumulated over several months to years, as compared with the instantaneous exposure received by the surivors of the atomic bombs in Japan. Studies of thyroid cancer in children exposed to iodine-131 might also contribute new knowledge. Cohort and case-control studies of workers and of populations living near Chernobyl remain the most promising way of obtaining quantitative information on the health risks from the accident.

JOHN BOICE
Branch chief
MARTHA LINET
Senior investigator

Epidemiology and Biostatistics Program,
National Cancer Institute,
Bethesda, MD 20892, USA

1 Commission of the European Communities, *Feasibility of studies on health Effects m western Europe due to the reactor accident at Chernobyl and recommendation for research.* Luxembourg: Commission of the European Communities, 1990. (Report EUR 12551.)
2 Committee on the Biological Effects of Ionizing Radiations, *Health effects of exposure* to *low levels of ionizing radiation (BEIR V).* Washington, DC: National Academy Press, 1990.
3 Parkin DM, Cardis E, Masuyer E, Friedl HP, Hansluwka, Bobev D, et al. Childhood leukaemia following the Chernobyl accident the European childhood leukaemia-lymphoma incident study ECLIS. *Eur J Cancer* 1993;29A:87-95.
4 Auvinen A, Hakama M, Arvela H, Hakulinen T, Rahola T, Suomela M, et al Fallout from Chernobyl and incidence of childhood leukaemia in Finland, 1976-92. *BMJ* 1994; 309: 151-4.
5 Hjalmars U, Kulldorff M, Gustafson G, for the Swedish Child Leukaemia Group. Fallout from the Chernobyl accident and risk of acute childhood leukaemia in Sweden. *BMJ* 1994; 309:1 54-7.
6 Ivanov EP, Tolochko G, Lazarev VS, Shuvaeva L, Childhood leukaemia after Chernobyl, *Nature* 1993;365:702.
7 Greenland S, Robins J. Invited commentary: ecologic studies—biases, misconceptions, and counterexamples. *Am J Epidemiol 1994; 139:747-60,*
8 Liner MS, Boice JD Jr. Radiation from Chernobyl and risk of childhood leukaemia. *Eur J Cancer* 1993;29A:1-3.
9 Land CE. Estimating cancer risks from low doses of ionizing radiation, *Science* 1980;209:1197-203.
10 Sperling K, Pelz O, Wegner R-D, Dorries A, Gruters A, Mikkelsen M. A significant increase of trisomy 21 in Berlin nine months after the Chernobyl accident: temporal correlation or casual relation? BMJ 1994;309:158-62.
11 Little J. The Chernobyl accident, congenital anomalies and other reproductive outcomes, *Paediatr Perinat Epidemiol* 1993;7:121-51.
12 Neel JV, Schull WJ, eds. *The children of atomic bomb survivors-a genetic study.* Washington, DC: National Academy Press, 1991.
13 Lie RT, Irgens LM, Skjaerven R, Reitan JB, Strand P, Strand T. Birth defects in Norway by levels of external and food-bawd exposure to radiation from Chernobyl. *Am J Epidemiol* 1992;136:377-88.